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Physical activity, dietary calcium to magnesium intake and mortality in the National Health and Examination Survey 1999–2006 cohort

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Abstract

Calcium and magnesium affect muscle mass and function. Magnesium and calcium are also important for optimal vitamin D status. Vitamin D status modifies the associations between physical activity and risk of incident cardiovascular disease (CVD) and CVD mortality. However, no study examined whether levels of magnesium and calcium and the ratio of dietary calcium to magnesium (Ca:Mg) intake modify the relationship between physical activity and mortality. We included 20,295 National Health and Nutrition Examination Survey participants (1999–2006) aged >20 years with complete dietary, physical activity and mortality data (2,663 deaths). We assessed physical activity based on public health guidelines and sex-specific tertiles of MET-minutes/week. We used Cox proportional hazards models adjusted for potential confounding factors and stratified by the intakes of magnesium, calcium, Ca:Mg ratio. We found higher physical activity was significantly associated with reduced risk of total mortality and cause-specific mortality, regardless of Ca:Mg ratio, magnesium or calcium intake. In contrast, both moderate and high physical activity were significantly associated with substantially reduced risks of mortality due to cancer when magnesium intake was above the RDA level. We also found higher physical activity was significantly associated with a reduced risk of mortality due to cancer only when Ca:Mg ratios were between 1.7 and 2.6, although the interaction was not significant. Overall, dietary magnesium and, potentially, the Ca:Mg ratio modify the relationship between physical activity and cause-specific mortality. Further study is important to understand the modifying effects of the balance between calcium and magnesium intake on physical activity for chronic disease prevention.

Keywords

physical activity; diet; mortality; calcium; magnesium; Ca:Mg ratio

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Additional Supporting Information may be found in the online version of this article.

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Introduction

Two previous reports indicate that physical activity may only be related to reduced risks of incident cardiovascular disease (CVD)[1] and mortality due to CVD[2] when serum levels of 25-hydroxyvitamin D (25(OH)D) were sufficient (20 to <30 ng/ml) or optimal (≥30 ng/ml). In particular, moderate physical activity was significantly associated with a reduced risk of incident CVD when serum 25(OH)D levels were optimal.[1] We reported earlier that magnesium intake significantly interacted with vitamin D intake affecting vitamin D deficiency and insufficiency.[3] Supporting this finding, we reported very recently from a randomized trial conducted among individuals with calcium: magnesium (Ca:Mg) ratios over 2.6 that reducing Ca:Mg ratios to around 2.3 through magnesium supplementation optimized vitamin D status.[4,5] Furthermore, we reported that serum vitamin D concentrations were associated with reduced risks of colorectal cancer and CVD mortality only when magnesium intake was high.[3] Previous studies also consistently linked physical activity to reduced risks of total mortality and mortality due to cancer and CVD.[6] Thus, it is likely that the associations between physical activity and risks of total mortality and mortality due to cancer and CVD differ by the status of Ca:Mg ratio, magnesium and/or calcium.

Insufficient dietary intake of nutrients such as calcium and magnesium may be associated with increased risk of cancer, CVD, metabolic disease and total mortality.[7,8] Second to calcium, magnesium is the most abundant divalent cation in the body and the nutrients can potentially antagonize each other in physiologic pathways, including skeletal muscle function.[9,10] Studies demonstrate that circulating, extracellular calcium and magnesium levels may influence skeletal muscle function[11] and potentially the quality of skeletal muscle, in addition to overall physical functioning.[12,13] In turn, low dietary calcium and magnesium, or the balance between the two, may influence an individual's ability to engage in the recommended levels of moderate-intensity physical activity, which may have significant effects on overall health and mortality.[14,15] However, no studies assessing the influence of dietary supplementation on muscle performance or physical functioning examined both nutrients.[13,16] Moreover, while the evidence for the influence of magnesium on physical performance and health across the lifespan are inconsistent, the evidence for the importance of the Ca:Mg in overall health is growing.[17-21]

Studies indicate that the balance between calcium and magnesium plays an essential role in skeletal muscle function and contractility.[13,22] Evidence from studies conducted in populations with high Ca:Mg ratios (medians ranging from 2.6 to over 3.0)[17-19,21,23-26] and those conducted in populations with low Ca:Mg ratio (median around 1.7)[10] suggests that a Ca:Mg ratio between 1.7 and 2.6 may be required for intakes of calcium and magnesium to be protective against colorectal cancer and, possibly, total mortality and mortality due to total cancer and CVD.[10] Despite this evidence, no studies have examined the interaction between the Ca:Mg ratio with physical activity in risk of mortality.

Since the Ca:Mg ratio, magnesium and/or calcium play central roles in muscle function and are associated with total mortality plus mortality due to CVD and cancer; we hypothesize that the Ca:Mg ratio and intakes of magnesium and calcium may modify the relationship between physical activity and mortality. To examine this novel hypothesis of effect modification by the Ca:Mg ratio, magnesium and calcium on the relationship between physical activity and mortality, we analyzed the data from the National Health and Nutrition Examination Survey (NHANES) 1999–2006 cohort.

Material and Methods

The NHANES study population is a continuous annual survey focused on the health and diet of the civilian, non-institutionalized U.S. population aged 2 months and older.[27] Each survey investigates a nationally representative sample using a multistage, stratified, clustered sampling strategy. Since physical activity was measured using the same methods across the NHANES 1999–2000, 2001–2002, 2003–2004 and 2005–2006 cycles, we used data from the NHANES 1999–2006 for this analysis and included 41,474 participants. We excluded 21,163 individuals from the study who were less than 20 years of age and 16 individuals missing physical activity measurements. As a result, in the final analysis, we included 20,295 adults with a total of 2,663 recorded deaths. Our study was approved by the National Center for Health Statistics Research Ethics Review Board and all subjects provided consent prior to enrollment.

According to NHANES 1999–2006, physical activity was measured using a specific “physical activity and physical fitness questionnaire” and includes questions related to daily activities, leisure time activities and sedentary activities at home.[27] In the mobile examination center, participants reported the physical activities that they have done in the past 30 days and the metabolic equivalent of task (MET) calculated. Each activity was assigned to a METs ranging from 0.9 (sleeping) to 18 METs (running at 10.9 miles per hour) by NHANES.[28] We calculated the variable for MET-minutes per week as a total of MET-minutes for each participant, based upon measures of frequency and duration by activity. We chose thresholds for physical activity groups using two methods. First, in order to align with accepted international thresholds, we used the World Health Organization guidelines for physical activity, which state that 500 MET-min or 1,000 MET-min (equivalent to approximately 8.33 and 16.67 MET-hr per week, respectively) can influence health and reduce risk of chronic disease.[29] Therefore, we defined four categories as (*i*) inactive (those without regular physical activity); (*ii*) insufficient (those performing less than 500 MET-min activity/week); (*iii*) moderate (those performing 500–1,000 MET-min activity/week; and (*iv*) high (those performing great than 1,000 MET-min activity/week). Second, in order to account for differences between men and women, we calculated sex-specific tertiles of the MET-minutes/week distribution. Participants who reported no regular physical activity in the past 30 days were again classified as Inactive, and the other three categories were low (performing <562 [men] or <371 [women] MET-min/week), moderate (performing 562–1,757 [men] or 371–1,200 [women] MET-min activity/week) and high (performing greater than 1,757 [men] or 1,200 [women] MET-min activity/week).

Baseline dietary intake was assessed using a dietary supplement questionnaire as well as a 24-hr dietary recall interviews, as described previously.[27] Daily supplemental intakes of calcium and magnesium over the past 30 days were determined based on the dietary supplement questionnaire conducted using the computer-assisted personal interviewing. We evaluated dietary intake alone and total intakes of these nutrients, which was calculated by taking the sum of intake from diet and supplements.

Longitudinal mortality outcomes were determined by using probabilistic linkage with the National Death Index through December 31, 2011, providing 6–12 years of follow-up for NHANES 1999–2006 participants. The median number of years of follow-up was 8.5 years. All-cause and cause-specific mortality were ascertained using both the Ninth Revision of the International Classification of Disease (ICD-9) and the Tenth Revision (ICD-10) cause of death coding for all U.S. deaths.[30] Nine cause-specific death categories were included in the public-use linked mortality files. In the current study, we included 2,663 deaths from all-cause, cancer and CVD specific mortality. Participants who died of other diseases or were not known deceased, were censored at the date of death or December 31, 2011, whichever was earlier.

We evaluated crude models (only adjusted for age and sex) along with several potential confounding factors including the following: race and ethnicity (Mexican Americans, other Hispanic, Non-Hispanic Whites, Non-Hispanic Blacks and other groups), education level (less than high school education diploma; high school diploma, including General Equivalent Diploma; and college graduate or above), poverty income ratio (<1, 1–4, ≥4), cigarette smoking status (never, former, current), alcohol use (never, former, current), self-reported history of angina, coronary heart disease, heart attack and shock (Yes or No), body mass index (BMI) and total dietary intakes of energy, magnesium and calcium). We also examined self-reported data on functional limitations caused by long-term mental health and comorbid conditions that could impact physical activity. We assessed confounding by using Rao–Scott chi-square test for categorical data and survey regression model for continuous variables.

We have conducted tests by using time-dependent explanatory variables to assess the proportional hazards assumptions for each model and found the proportional hazards assumption was met. We used Cox proportional hazards models to investigate the association between physical activity and mortality, adjusting for potential confounding factors. We evaluated tests for trends by entering the categorical variables as continuous variables in the model and interactions using the likelihood ratio test. We conducted stratified analyses by Ca:Mg intake ratio (i.e., 2.6), the calcium dietary reference intakes (DRI; 1,000 mg/day), the magnesium Recommended Dietary Allowance (RDA; 320 mg/day for women and 420 mg/day for men). We also conducted joint analyses for calcium and magnesium. The threshold for the Ca:Mg intake ratio was used based on the previous studies conducted in multiple, diverse populations.[10,17,19,21,31] We performed all the statistical analyses using Survey procedure in SAS 9.4 software (SAS Institute, Cary, NC) to estimate variance after incorporating the weights for the sample population, which take into account unequal selection probabilities and planned oversampling of certain subgroups in NHANES. We set statistically significant at $\alpha = 0.05$ and all p values were two-tailed.

Data availability

All data will be made available upon request.

Results

Table 1 presents selected demographic characteristics and potential confounding by level of physical activity. NHANES participants in the current study with the lowest physical activity were older (mean age 50.1 years) and more likely to be Mexican American or Black. Moreover, those reporting the lowest physical activity were more likely to smoke, use alcohol, as well as have less education and lower income. In addition, energy intake was lowest among participants reporting low physical activity, while the frequency of obesity was highest in this group. The frequency of participants who were categorized as "overweight" by BMI increased with increasing physical activity. Finally, we observed a trend of increasing calcium and magnesium intake with higher reported physical activity.

In Table 2, the results demonstrate that engaging in physical activity at a level at or above public health recommendations was associated with reduced risk of overall mortality from any cause, as well as death from cardiovascular disease and cancer, specifically. For all-cause mortality, moderate (500–1,000 MET-min/week) or high (>1,000 MET-min/week) physical activity were associated with a 28 and 38% reduction in mortality risk, respectively. Among participants reporting the highest levels of physical activity, we observed a 50% reduction in CVD mortality risk using public health guideline cutpoints (Hazard Ratio (HR) 0.50 (95% confidence interval [CI] 0.35, 0.71). Similarly, using sex-specific tertiles, a greater reduction of risk, 62%, was observed (HR 0.38 (95% CI 0.22, 0.65). For cancer, we observed similarly reduced risk for those engaging in high levels of physical activity with both public health guidelines and sex-specific tertiles (HR 0.68 [95% CI 0.53, 0.89] and HR 0.60 [95% CI 0.44, 0.84], respectively).

The results from the stratified analyses by Ca:Mg ratio and intakes of magnesium and calcium are presented in Table 3. Using sex-specific tertiles, we found that higher physical activity level was significantly associated with reduced risk of all-cause mortality and mortality due to CVD regardless of Ca:Mg ratios. However, higher physical activity was only significantly associated with a reduced risk of mortality due to cancer among those with Ca:Mg ratios <2.6, with a hazard ratio of 0.48 (95% CI 0.26, 0.87) comparing the highest tertile of physical activity to the lowest. The corresponding HR (95% CI) was further reduced to 0.40 (0.19, 0.84) after excluding those with Ca:Mg ratios <1.7 (data not shown). Physical activity was not associated with risk of mortality due to cancer among individuals reporting a higher Ca:Mg intake ratio (>2.6). The results using public health guidelines and dietary intake demonstrate similar trends (Supporting Information Tables S1 and S2). Moreover, results adjusted by comorbid conditions are presented in Supporting Information Table S3 and are similar to the unadjusted results.

In additional stratified analyses by intakes of magnesium and calcium (Table 3), including joint analyses crude models (Supporting Information Tables S4 and S5), we found that higher physical activity level was associated with a reduced risk of total mortality regardless of calcium and magnesium levels. We found higher physical activity was associated with reduced risk of mortality to due to CVD regardless of magnesium intake. However, physical activity significantly interacted with intakes of magnesium (p for interaction, 0.02) affecting risk of mortality due to cancer. When magnesium intake was above the RDA level, we found that moderate and high physical activity were significantly associated with 58 and 53% reduced risks of mortality due to cancer, respectively. We also found that higher physical activity level was linked to a decreased risk of mortality due to cancer regardless of calcium intake level, but was associated with a reduced risk of mortality due to CVD only when calcium intake was above the DRI level, with a corresponding HR (95% CI) of 0.22 (0.09, 0.55; *p*-interaction = 0.09).

Discussion

In the current study, for the first time, we found evidence to support the hypothesis that intake of magnesium may interact with physical activity levels on risk of cancer mortality. Overall, we found higher physical activity level was significantly associated with a reduce risk of total mortality, regardless of Ca:Mg ratio, magnesium intake or calcium intake. In contrast, we observed that physical activity significantly interacted with magnesium intake affecting risk of mortality due to cancer. We found both moderate physical activity and high physical activity were significantly associated with substantially reduced risks of mortality due to cancer when magnesium intake was above the RDA level. We also ran additional stratified analyses by the joint Ca and Mg categories. Although the sample sizes became sparse in some strata in the stratified analyses by joint levels of Ca and Mg, these associations indicate physical activity at either moderate or high level has the highest reduction in risk of mortality due to cancer among those with high Mg intake (i.e., male≥420 or female≥320 mg/day) and high Ca intake (i.e., ≥1,000 mg/day), while physical activity at either moderate or high level has the greatest reduction in risk of mortality due to CVD among those with high Mg intake (i.e., male ≥ 420 or female ≥ 320 mg/day) and low Ca intake (i.e., <1,000 mg/day). This finding is consistent with our finding that higher physical activity was significantly associated with a reduced risk of mortality due to cancer only when Ca:Mg ratios were between 1.7 and 2.6, although the interaction was not significant. We also found higher physical activity level was significantly linked to a decreased risk of mortality due to CVD only when intake of calcium was above DRI level, but the interaction test was not statistically significant.

Previous studies support the role of dietary calcium and magnesium in skeletal muscle and overall physical functioning.[13,22] Magnesium intake was associated with physical functioning, while both were associated with prevalence of sarcopenia.[13] Moreover, a recent intervention study conducted among elderly women found that magnesium supplementation significantly improved physical performance.[16] In contrast, Soria *et al*. recently demonstrated that exercise among endurance athletes with sufficient magnesium intake did not alter circulating magnesium concentrations.[32] Among elderly, sarcopenia and lower physical functioning may reduce the likelihood of engaging in higher-intensity physical activity. These studies suggest that the influence of dietary magnesium on muscle mass and physical functioning may also be related to both age and previous exercise history. In addition, a recent meta-analysis demonstrated that calcium intake is significantly associated with muscle mass in older adults.[13]

Thus, our novel findings are biologically plausible because body status of magnesium, calcium and their balance are critical for muscle mass and function. In particular, we found when magnesium intake was above the RDA level, moderate physical activity was associated with a reduced risk of mortality due to cancer; and also high physical activity was more strongly associated with a reduced risk compared to those with magnesium intake below the RDA. These findings are consistent with our finding that high physical activity was associated with a reduced risk only when Ca:Mg ratios were lower (i.e., between 1.7 and 2.6). It is likely that a lower Ca:Mg ratio is mainly due to a higher intake of magnesium. Consistent with that from an observational study, we found in a randomized trial that reducing Ca:Mg ratios to around 2.3 through magnesium supplementation optimized vitamin D status among individuals with Ca:Mg ratios over 2.6.[5] Thus, in addition to muscle function, adequate magnesium intake levels or Ca:Mg ratios could lead to optimal vitamin D status. Further, previous studies found physical activity may only be related to reduced risks of incident CVD[1] and mortality due to CVD[2] when serum levels of 25(OH)D were sufficient (20 to <30 ng/ml) or optimal (≥30 ng/ml) while moderate physical activity was significantly associated with a reduced risk of incident CVD only when serum 25(OH)D levels were optimal.[1] Although there is no exiting study on cancer outcomes, taken together, it is possible that magnesium levels above RDA are critical for optimal vitamin D status and, in turn, for the beneficial effect of moderate physical activity.

In addition, one striking observation from animal studies is that calcium-adequate and magnesium-deficient diets (i.e., a higher Ca:Mg ratio lead to increases in inflammatory responses, heart lipid peroxidation and triglyceride levels.[33] Conversely, diets deficient in both calcium and magnesium cause a normalization of heart lipid peroxidation, inflammatory responses and dyslipidemia.[33] Although not consistent, magnesium is associated with blood pressure and believed to act by improving endothelial function, reducing vascular inflammation and platelet aggregation/clot formation.[31] Moreover, in addition to the potential of both calcium and magnesium to influence immune function and inflammation, magnesium also plays a role in DNA synthesis and repair as well as insulin regulation, all of which are critical pathways related to carcinogenesis.[21,34] These findings highlight the critical role of the dietary magnesium, calcium and their balance in the development of chronic inflammation, oxidative stress and dyslipidemia-related diseases, such as type 2 diabetes, cardiovascular disease and cancer.

We previously found that Ca:Mg intake ratios modified the associations between intakes of calcium and magnesium and risks of gastrointestinal neoplasia,[17,21] total mortality and mortality due to CVD and cancer.[10] In contrast to the findings from studies conducted in U.S. populations with high Ca:Mg intake ratios, in Chinese populations with low Ca:Mg intake ratios (median ratio around 1.7), magnesium intake ≥ the RDA (≥320 mg/day for women and ≥420 mg/day for men) was associated with an increased risk of total mortality and mortality due to cardiometabolic disease for both men and women.[10] This finding is consistent with the Japan Collaborative Cohort Study which was also conducted in a population with similarly low Ca:Mg ratios and found that magnesium intake was significantly related to an increased risk of total stroke in women with an HR (95% CI) of 1.81 (1.12, 2.94) for the highest quintile intake *vs*. the lowest (p for trend = 0.02) in the fully adjusted model.[31] These human findings suggest that the effects of magnesium intake may largely depend on the background Ca:Mg intake ratio.[10] However, the mechanism is unclear. In our study, we observed that physical activity may protect against mortality due to CVD and cancer only when intakes of calcium and magnesium are above DRI and RDA levels, respectively, and Ca:Mg ratios are between 1.7 and 2.6.

Studies have also assessed the role of calcium and magnesium, independently, on mortality. For example, in a recent meta-analysis, Asemi *et al.* reported an inverse association between long-term dietary calcium intake and reduced CVD and cancer mortality.[8] In addition, supplemental calcium intake was inversely associated with total mortality, but not cause-specific.[8] Moreover, Chiuve *et al.* found that higher dietary magnesium intake (>342 mg/day) was associated with reduced risk of death from coronary heart disease (RR 0.61 95% CI 0.45, 0.84).[26] Deng *et al.* also demonstrated in the NHANES population that higher magnesium intake (>264 mg/day) was associated with reduced risk of CVD mortality, but in contrast not total or colorectal cancer mortality.[3] However, while these studies may have adjusted for either calcium magnesium intake as a potential confounding factor, none assessed the balance between the nutrients or potential interactions by physical activity level.

The strengths of our study include the prospective nature of NHANES, the overall large sample size and a population-based study with nationally representative samples as well as the detailed evaluation of dietary and lifestyle factors. However, there were also limitations to the results. While there are at least 50 deaths per each strata evaluated in Table 2, the overall sample size for deaths in our study is relatively small. This may have influenced the nonstatistically significant interaction, observed in the current study. Moreover, the National Death Index data are limited and no detail on the disease or treatment information was available. In addition, although multiple 24-hr dietary recalls are used as a gold standard measure in nutritional epidemiologic studies, a one-time 24-hr dietary recall may not capture long-term dietary exposure. Also, physical activity was not objectively measured and change over time was not accounted for, thus there is the potential for misclassification. However, for dietary intake, since change in dietary intake could lead to inter-day variation in intakes of magnesium and calcium and physical activity at random, any residual inter-day variation may lead to nondifferential misclassification, which usually biases the result to the null. Thus, the true associations may be stronger than those we observed. Finally, our findings are biologically plausible, indicating our findings may not be solely due to chance.

Dietary intake of calcium and magnesium and their balance are demonstrated to be central to multiple physiologic functions and influence overall health, including muscle function and mass. The results of the current study suggest that magnesium above the RDA level is necessary for the protective effect of physical activity, specifically moderate physical activity, on mortality, particularly mortality due to cancer. Further evaluation of the influence of intakes of magnesium and calcium as well as the Ca:Mg ratio on physical activity and physical performance across the life span are necessary and may provide inside into the integrative prevention strategies combining physical activity with optimal nutritional status for the prevention of chronic diseases.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

Ca	calcium
CVD	cardiovascular disease
DRI	dietary reference intakes
HR	hazard ratio
MET	metabolic equivalent units
Mg	magnesium
NHANES	National Health and Nutrition Examination Survey
RDA	recommended dietary allowance

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What's new?

Calcium and magnesium are fundamental to the metabolism of vitamin D, which in turn influences relationships between physical activity and mortality. Whether calcium and magnesium also modify physical activity effects on mortality, similar to vitamin D, remains unknown. Here, higher levels of physical activity were associated with reduced risk of overall mortality and mortality from cardiovascular disease and cancer. Magnesium intake above the recommended daily allowance level was critical to the preventive effect of moderate and high physical activity on cancer mortality. Calcium intake and balanced calcium and magnesium intake may also influence interactions between physical activity and mortality risk.

Table 1.

Characteristics of the NHANES 1999–2006 participants at baseline

	Physical activity guidelines[1]			
Characteristics	**Inactive (*n* = 9,179)**	**Insufficient (*n* = 3,913)**	**Moderate (*n* = 2,257)**	**High (*n* = 4,946)**
Age at screening[2]	50.1 (49.5–50.8)	44.9 (44.1–45.7)	45.6 (44.7–46.5)	42.7 (41.9–43.6)
Gender: male	3,775 (44.9)	1,573 (42.9)	1,040 (47.9)	2,631 (55.4)
Race/ethnicity				
Mexican American	2,320 (10.5)	713 (6.6)	399 (5.8)	733 (5.1)
Other Hispanic	382 (6.1)	137 (4.0)	81 (4.6)	188 (5.0)
Non-Hispanic, White	3,511 (64.1)	2,040 (74.6)	1,264 (77.1)	2,669 (76.0)
Non-Hispanic, Black	1,928 (14.3)	675 (9.5)	335 (8.0)	899 (9.4)
Other Race[3]	282 (5.1)	162 (5.3)	87 (4.6)	178 (4.5)
Education level				
Less than high school	3,844 (32.7)	898 (15.9)	416 (12.0)	821 (10.7)
High school including GED	2,082 (29.7)	895 (25.0)	527 (25.8)	1,003 (21.6)
Some college or above	2,471 (37.6)	1,929 (59.1)	1,222 (62.2)	2,838 (67.7)
Poverty income ratio				
<1	1,879 (19.4)	547 (11.2)	242 (8.4)	546 (9.0)
1–4	4,398 (57.0)	1,892 (51.1)	1,037 (46.7)	2,159 (45.4)
≥4	1,304 (23.6)	1,058 (37.7)	752 (44.9)	1,683 (45.6)
BMI, (kg/m^1)				
BMI < 18.5	139 (2.0)	55 (2.0)	41 (2.0)	65 (1.6)
18.5 ≤ BMI < 25	2,217 (29.1)	1,059 (30.0)	657 (32.9)	1,592 (37.7)
25 ≤ BMI < 30	2,799 (32.4)	1,263 (33.8)	781 (35.2)	1,681 (35.6)
BMI ≥ 30	2,872 (36.4)	1,279 (34.1)	643 (29.9)	1,245 (25.1)
Smoking status				
Nonsmoker	4,110 (45.3)	1,998 (51.8)	1,149 (52.1)	2,568 (55.0)
Former-smoker	2,194 (24.8)	958 (24.5)	607 (27.4)	1,227 (24.9)
Current-smoker	2,101 (30.0)	768 (23.7)	410 (20.5)	869 (20.2)
Alcohol use				

Characteristics	Physical activity guidelines[1] Inactive (*n* = 9,179)	Insufficient (*n* = 3,913)	Moderate (*n* = 2,257)	High (*n* = 4,946)
No drinker	1,383 (15.4)	491 (11.8)	237 (9.9)	484 (9.8)
Former drinker	2,036 (24.0)	673 (16.9)	330 (14.0)	644 (11.4)
Current drinker	4,185 (60.5)	2,288 (71.2)	1,447 (76.1)	3,220 (78.8)
CVD[4]	1,174 (11.8)	333 (7.2)	196 (6.4)	289 (4.9)
Type 2 diabetes[5]	1,223 (11.6)	403 (7.7)	197 (625)	352 (6.1)
Energy (kcal/day)	2,112.9 (2,074.7–2,151.1)	2,209.8 (2,166.9–2,252.6)	2,237.2 (2,183.3–2,291.2)	2,331.8 (2,289.4–2,374.2)
Total calcium (mg/day)	987.3 (963.5–1,011.1)	1,095.3 (1,063.3–1,127.3)	1,200.1 (1,160.1–1,240.1)	1,221.1 (1,175.5–1,266.7)
Total magnesium (mg/day)	302.0 (295.5–308.4)	330.0 (320.7–339.3)	350.6 (338.4–362.7)	374.8 (362.8–386.7)

[1]Guideline-based categories: Inactive (no reported regular activity); insufficient (>0 to <500 MET-min/week); moderate: (500–1,000 MET-min/week); and high (>1,000 MET-min/week).

[2]Continuous variables summarized as mean (95% CI), categorical variables as n (%).

[3]"Other Race" includes individuals reporting multiple races.

[4]CVD: defined as self-reported history of angina, coronary heart disease, heart attack and shock.

[5]Diabetes: defined as self-reported history of diabetes.

Table 2.

Associations between physical activity and mortality, NHANES 1999–2006

	Deaths/person-year	All-cause HR (95% CI)	*p*-trend	Deaths/person-year	CVD HR (95% CI)	*p*-trend	Deaths/person-year	Cancer HR (95% CI)	*p*-trend
Physical activity guidelines[1]									
Inactive	1,748/65,009	REF		471/65,009	REF		365/65,009	REF	
Insufficient	354/29,345	0.69 (0.59, 0.82)		83/29,346	0.57 (0.41, 0.80)		83/29,346	0.66 (0.46, 0.95)	
Moderate	216/17,551	0.72 (0.60, 0.87)		61/17,551	0.84 (0.57, 1.25)		58/17,551	0.84 (0.58, 1.22)	
High	345/38,225	0.62 (0.53, 0.73)	<0.001	70/38,225	0.50 (0.35, 0.71)	0.004	97/38,225	0.68 (0.53, 0.89)	0.007
Physical activity sex-specific tertiles[2]									
Inactive	1,748/65,009	REF		471/65,009	REF		365/65,009	REF	
Low	360/27,427	0.72 (0.61, 0.86)		360/27,427	0.61 (0.44, 0.85)		86/27,427	0.71 (0.50, 1.02)	
Moderate	342/29,026	0.72 (0.61, 0.85)		96/29,026	0.77 (0.55, 1.06)		86/29,026	0.79 (0.56, 1.11)	
High	213/28,668	0.55 (0.45, 0.67)	<0.001	36/28,668	0.38 (0.22, 0.65)	<0.001	66/28,668	0.60 (0.44, 0.84)	0.001

Cox proportional hazards models were performed with the SAS SURVEYPHREG procedure to estimate odds ratios and 95% confidence intervals, adjusting for: age, sex, race-ethnicity, education, poverty income ratio, smoking, alcohol use, BMI, total intake of energy, calcium and magnesium.

[1] Guideline-based categories: inactive (no reported regular activity), insufficient (>0 to <500 MET-min/week), moderate: (500–1,000 MET-min/week) and high (>1,000 MET-min/week).

[2] Sex-specific tertiles: inactive, low (performing <562 (men) or <371 (women) MET-min/week), moderate (performing 562–1,757 [men] or 371–1,200 [women] MET-min activity/week) and high (performing greater than 1,757 [men] or 1,200 [women] MET-min activity/week).

Table 3.

Associations between sex-specific tertiles of physical activity and mortality stratified by the intake of calcium, magnesium or calcium to magnesium ratio

	Deaths/person-year	All-cause HR (95% CI)	*p*-trend	Deaths/person-year	CVD HR (95% CI)	*p*-trend	Deaths/person-year	Cancer HR (95% CI)	*p*-trend
Ca:Mg < 2.6									
Inactive[2]	727/26,990	REF		193/26,990	REF		165/26,990	REF	
Insufficient	160/10,176	0.77 (0.58, 1.02)		40/10,176	0.78 (0.45, 1.34)		32/10,176	0.48 (0.26, 0.87)	
Moderate	146/11,039	0.71 (0.56, 0.91)		41/11,039	0.77 (0.50, 1.20)		39/11,038	0.80 (0.50, 1.27)	
High	82/10,787	0.55 (0.39, 0.77)	<0.001	15/10,787	0.27 (0.12, 0.65)	0.001	27/10,787	0.48 (0.26, 0.87)	0.01
Ca:Mg ratio ≥ 2.6									
Inactive	1,011/37,961	REF		273/37,961	REF		199/37,961	REF	
Insufficient	198/17,221	0.68 (0.55, 0.84)		42/17,221	0.50 (0.32, 0.78)		54/17,221	0.86 (0.57, 1.30)	
Moderate	196/17,957	0.73 (0.57,0.93)		55/17,958	0.80 (0.49, 1.30)		47/17,957	0.77 (0.47, 1.27)	
High	130/17,869	0.54 (0.42, 0.69)	<0.001	21/17,869	0.43 (0.25, 0.73)	0.005	39/17,869	0.68 (0.44, 1.05)	0.06
p-interaction[1]									
Magnesium: male < 420 or female < 320 mg/day									
Inactive	1,423/48,713	REF		387/48,713	REF		288/48,713	REF	
Insufficient	270/19,122	0.68 (0.56, 0.82)		60/19,122	0.48 (0.32, 0.72)		66/19,122	0.79 (0.54, 1.17)	
Moderate	259/18,899	0.80 (0.66, 0.97)		73/18,899	0.84 (0.60, 1.16)		69/18,899	1.00 (0.69, 1.45)	
High	150/17,922	0.53 (0.43, 0.65)	<0.001	26/17,922	0.37 (0.22, 0.64)	0.002	49/17,922	0.66 (0.45, 0.96)	0.08
Magnesium: male ≥ 420 or female ≥ 320 mg/day									
Inactive	325/16,296	REF		84/16,296	REF		77/16,296	REF	
Insufficient	90/8,305	0.81 (0.59, 1.11)		22/8,305	1.01 (0.52, 1.97)		20/8,305	0.52 (0.27, 1.01)	
Moderate	83/10,127	0.56 (0.44, 0.72)		23/10,127	0.65 (0.35, 1.21)		17/10,127	0.42 (0.22, 0.81)	
High	63/10,747	0.57 (0.39, 0.82)	<0.001	10/10,747	0.40 (0.16, 0.98)	0.02	17/10,747	0.47 (0.23, 0.98)	0.01
p-interaction[1]			0.09			0.10			0.02
Calcium < 1,000 mg/day									
Inactive	1,243/41,780	REF		327/41,780	REF		255/41,780	REF	
Insufficient	218/15,067	0.67 (0.53, 0.83)		52/15,067	0.55 (0.37, 0.84)		47/15,067	0.56 (0.35, 0.88)	
Moderate	211/15,073	0.79 (0.65, 0.96)		63/15,073	0.87 (0.62, 1.23)		53/15,073	0.87 (0.59, 1.28)	
High	120/14,427	0.65 (0.49, 0.85)	<0.001	25/14,427	0.56 (0.30, 1.06)	0.04	39/14,427	0.69 (0.43, 1.11)	0.07
Calcium ≥ 1,000 mg/day									

	Deaths/person-year	All-cause HR (95% CI)	*p*-trend	Deaths/person-year	CVD HR (95% CI)	*p*-trend	Deaths/person-year	Cancer HR (95% CI)	*p*-trend
Inactive	545/23,508	REF		255/23,508	REF		114/23,508	REF	
Insufficient	148/12,492	0.78 (0.61, 0.99)		47/12,492	0.65 (0.41, 1.03)		39/12,492	0.90 (0.52, 1.59)	
Moderate	139/14,078	0.66 (0.50, 0.86)		53/14,078	0.65 (0.36, 1.17)		35/14,078	0.75 (0.44, 1.26)	
High	95/14,361	0.45 (0.33, 0.61)	<0.001	39/14,361	0.22 (0.09, 0.55)	0.003	28/14,361	0.53 (0.30, 0.94)	0.02
p-interaction[1]			0.10			0.09			0.34

Cox proportional hazards models were performed with the SAS SURVEYPHREG procedure to estimate odds ratios and 95% confidence intervals, adjusting for age, sex, ethnicity, education, poverty income ratio, smoking, alcohol use, BMI, total intake of energy, calcium and magnesium.

[1]The *p* values are the interactions between the intakes of magnesium, or calcium, or calcium/magnesium ratio (continuous) with physical activity (categorical).

[2]Sex-specific tertiles: inactive, low (performing < 562 (men) or <371 (women) MET-min/week), moderate (performing 562–1,757 [men] or 371–1,200 [women] MET-min activity/week) and high (performing greater than 1,757 [men] or 1,200 [women] MET-min activity/week).